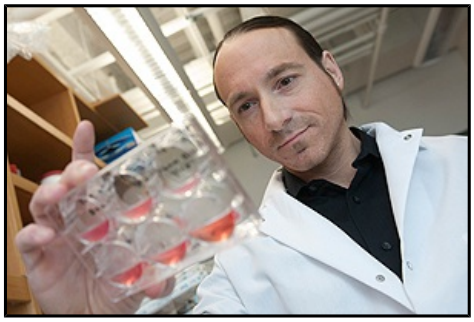
New approach creates red blood cells, platelets *in vitro*

By Marisa Naujokas



Murphy is head of a basic science and translational laboratory in the hematology and oncology section at BUSM. (Photo courtesy of Vernon Doucette)

An unlimited number of red blood cells and platelets can be generated from induced pluripotent stem (iPS) cells *in vitro*, according to a recent study *(http://bloodjournal.hematologylibrary.org/content/early/2013/05/29/blood-2012-11-466722.full.pdf+html?hw-tma-check=true)* out of the Boston University School of Medicine (BUSM) and School of Public Health (BUSPH), funded in part by NIEHS. This method could provide red blood cells and platelets for research and therapies, while also reducing the need for blood donations to treat patients requiring blood transfusions.

George Murphy, Ph.D., *(http://www.bumc.bu.edu/hematology/research/george-murphy-phd/)* assistant professor of medicine and co-director of the Center for Regenerative Medicine at BUSM, led the study, in collaboration with researcher David Sherr, Ph.D., *(http://sph.bu.edu/index.php?option=com_sphdir&id=239&Itemid=340&INDEX=676)* professor of environmental health at BUSPH and deputy director of the NIEHS-funded Boston University Superfund Research Program. The report was published online May 30 in the journal Blood.

Sherr is also director of the Immunology Training Program, and a member of the Hematology/Oncology Training Program, the Cancer Center, and the Amyloid Treatment and Research Center at Boston University. (Photo courtesy of Kalman Zabarsky)

"This finding has enabled us to overcome a major hurdle in terms of being able to produce enough of these cells to have a potential therapeutic impact both in the lab and, down the line, in patients," said Murphy.

From stem cells to red blood cells and platelets

Previous research has shown that iPS cells can be generated by reprogramming normal adult cells, such as skin or blood cells, into a more primitive stem cell state. From this stem cell state, they can then be pushed to differentiate into other cell types, such as hematopoietic cells, which are blood cell precursors.

In this study, researchers used growth factors and a patented technology to push iPS cells to differentiate into red blood cells and platelets. A new twist in their investigation revealed one mechanism that contributes to this differentiation — signaling through the aryl hydrocarbon receptor (AhR). The AhR pathway is involved in cellular proliferation and differentiation in many cell types, including tumor cells. Some environmental toxins, such as dioxins, can stimulate the AhR, and are linked to a number of adverse health effects, including cancer. In this study, modulating the AhR receptor in the iPS cells drove an unprecedented rapid increase in the number of new red blood cells and platelets *in vitro*. These results open the door to the possibility of generating large numbers of cells for research and therapeutic purposes.

Implications for therapeutics and blood supplies

When created from a patient's own cells, these iPS-derived blood cells are not viewed by the immune system as foreign material and may be used in therapies without concern for an immune response against the cells. They, therefore, have the potential to be a powerful tool in therapy for blood-related illnesses, such as malaria and blood-clotting disorders. This method of generating cells could also help offset blood supply shortages. Meeting the demand for blood transfusions can be challenging, particularly in the wake of natural or man-made disasters. A recent study *(http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2914428/)* out of Germany predicts that increasing demands for blood products could put a significant strain on blood supplies by 2050.

"Patient-specific red blood cells and platelets derived from iPS cells, which would solve problems related to immunogenicity and contamination, could potentially be used therapeutically, and decrease the anticipated shortage and the need for blood donations," added Murphy.

Citation: Smith BW, Rozelle SS, Leung A, Ubellacker J, Parks A, Nah SK, French D, Gadue P, Monti S, Chui DH, Steinberg MH, Frelinger AL, Michelson AD, Theberge R, McComb ME, Costello CE, Kotton DN, Mostoslavsky G, Sherr DH, Murphy GJ. *(http://www.ncbi.nlm.nih.gov/pubmed/23723449)* 2013. The aryl hydrocarbon receptor directs hematopoietic progenitor cell expansion and differentiation. Blood; doi:10.1182/blood-2012-11-466722 [Online 30 May 2013].

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The Environmental Factor is produced monthly by the National Institute of Environmental Health Sciences (NIEHS) *(http://www.niehs.nih.gov/)*, Office of Communications and Public Liaison. We welcome your comments and suggestions. *(bruskec@niehs.nih.gov)*

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